Signature: © Pol J Radiol, 2009; 74(1): 59-64

Polish Journal of Radiology
www.PolRadiol.com
REVIEW ARTICLE

Received: 2008.11.20
Accepted: 2009.01.12

Virchow-Robin spaces – an anatomic variant or a pathologic sign?

Iwona Łachmacka[1], Eugeniusz Tarasów[1], Elżbieta Gościk[2], Andrzej Lewszuk[1], Jerzy Walecki[3]

[1] Department of Radiology, Medical University of Białystok, Białystok, Poland
[2] Department of Pediatric Radiology, University Pediatric Clinical Hospital in Białystok, Białystok, Poland
[3] Polish Academy of Sciences, Medical Research Centre,Warsaw, Poland

Author's address: Iwona Łachmacka, Department of Radiology, Medical University of Białystok, M. Sklodowskiej-Curie 24a Str., 15-276 Białystok, Poland, e-mail: iwona.lachmacka@wp.pl

Summary

Virchow-Robin spaces surround blood vessels. Their walls are formed by prolongations of the pia mater and they have no communication with the subarachnoid space. VRS are often seen as well-delineated foci of cerebrospinal fluid signal on MR images. They are often located at the basal ganglia level, aggregating around anterior brain commissure. They are also found in the midbrain, hemisphere white matter and insular cortex. In spite of the fact, that VRS are described in usual radiological practice, there is no uniform definition of the dilated and normal forms of VRS. In this paper, we present the etiology, pathogenetic aspects and current opinions concerning Virchow-Robin spaces, based on the literature data and own clinical cases.

Key words: perivascular spaces • Virchow-Robin spaces • magnetic resonance imaging

PDF file: http://www.polradiol.com/fulltxt.php?ICID=879261

Perivascular spaces were described by Pestalozzi, and subsequently by Virchow in 1851 and Robin in 1859 year [1]. Virchow described VRS as the spaces between the adventitia and the lamina propria of cerebral blood vessels, which are currently regarded as the layers of pia mater. Robin confirmed Virchow's observations, but, unlike the former author, regarded VRS as closed canals located within the vascular walls. Both investigators coincidentally described the spaces which today are considered to correspond with perivascular spaces [2].

Virchow-Robin spaces (VRS) are currently defined as the spaces surrounding arterial blood vessels penetrating the brain tissue. The spaces are surrounded by the pia mater and filled with interstitial fluid, but they do not communicate directly with the subarachnoid space. Kwee et al. [3] distinguished 3 types of VRS. Type I includes the spaces arranged along the lenticulostriate arteries entering the basal ganglia through the anterior perforated substance. Type II includes the spaces situated along the spinal perforating arteries, penetrating the cerebral cortex in the superficial region of the brain and entering the white matter. Type III is observed in the midbrain.

Location-related differences in VRS structure are important. As demonstrated by electronic microscopy studies, the pia mater on the brain surface is arranged along the course of blood vessels in the subarachnoid space, separating the perivascular spaces from the interstitial space (below the pia mater) and from the subarachnoid space [4]. It has also been confirmed by MRI, in which quantitative measurements demonstrated differences between signal intensities of the fluid filling VRS and the cerebrospinal fluid (CSF) [5]. Within the cerebral cortex, VRS are located between a single layer of the pia mater and the arterial walls, whereas in the basal nuclei they are surrounded by a double layer of the pia mater, separating them from the subarachnoid space [6].

In CT, VRS are round, oval or linear in shape and are visible as point-like foci of low density, equal to attenuation of the CSF, showing no enhancement after contrast administration. However, dilatation of the perivascular spaces is usually difficult to demonstrate by CT [7].

In MRI, VRS are most frequently visualized in the basal nuclei of the brain, forming agglomeration around the ante-

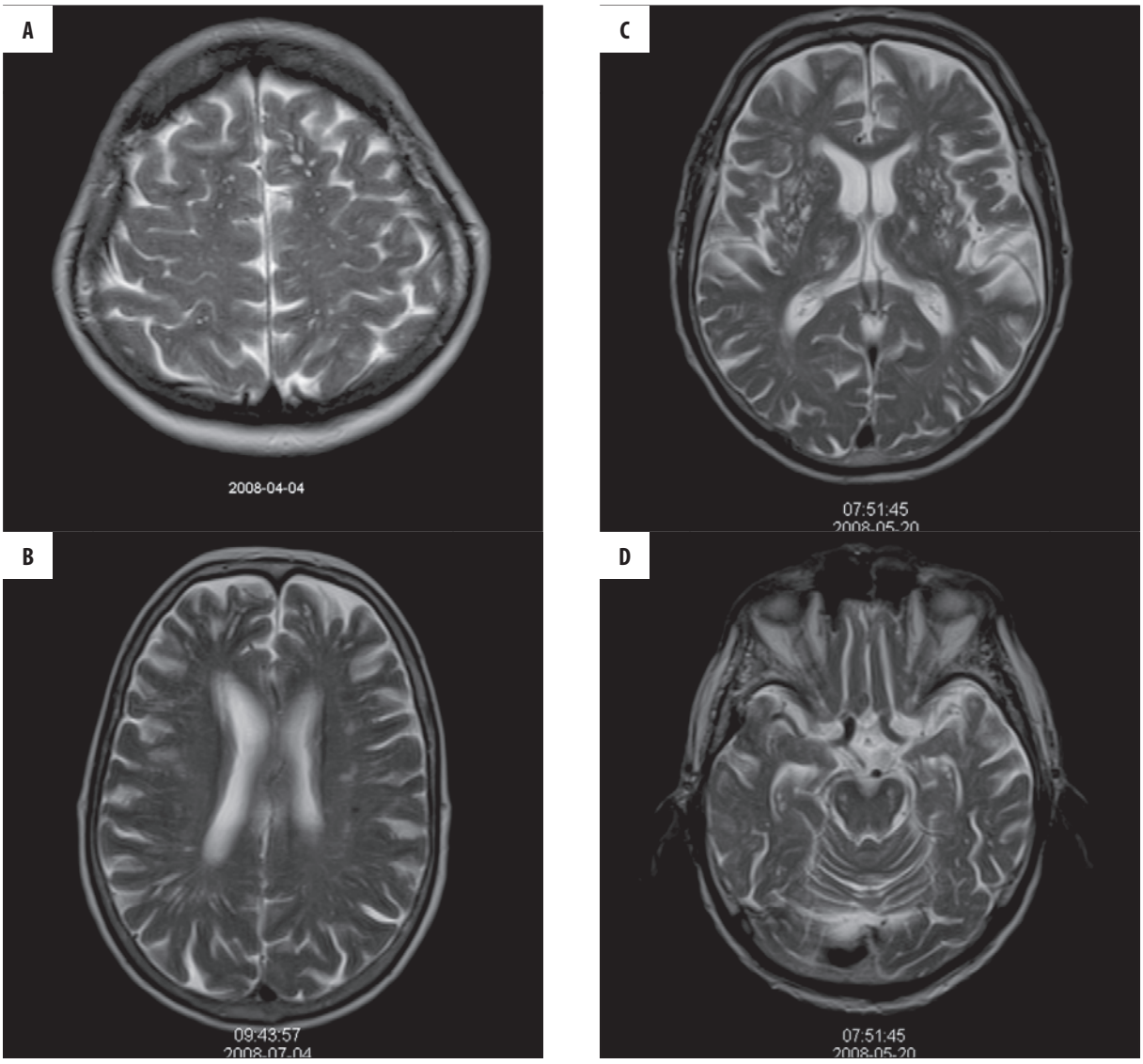

Figure 1. Normal Virchow-Robin spaces in the high-convexity white matter (**A**), creating typical "tailed" structures at the lateral ventricles level (**B**). In most cases VRS are localized in the basal ganglia (**C**), they are rarely seen in the brainstem (**D**).

rior commissure and in the midbrain, white matter of the cerebral hemispheres, the insular cortex and the internal capsule (Figure 1A–C) (8). They are visible less frequently in the thalamus, dentate nuclei, corpus callosum or cingulated gyrus. VRS are present also in other cerebral regions (Figure 1D); Gross et al. [9] described dilated VRS observed in a microscopic study in the medulla oblongata.

In T1- and T2-weighted MR images, VRS are usually visualized as multiple, well-delineated cyst-like structures isointense with cerebrospinal fluid. Comparative imaging and pathologic studies by Elster et al. [10] provide evidence indicating that hyperintense foci observed in MRI in the midbrain region correspond to perivascular areas of the penetrating arterial branches. In FLAIR sequences, VRS are completely suppressed. Additionally, in 25% of cases discrete reduction of signal intensity can be observed in the cerebral tissue surrounding dilated VRS. In DWI studies no definite signs of diffusion are observed within the perivascular spaces [11].

Fine VRS up to 2 mm in diameter are present in healthy subjects of all age groups [3]. Elster et al. [10] found them in the midbrains of 32/157 (20%) subjects. In contrast, in a study by Groeschel et al. [2] who examined 125 healthy subjects aged 1–30 years, VRS were visible in all cases; in children aged 2–16 years they were found with high frequency, reaching 80%.

Increased occurrence of VRS, often exceeding 2 mm in diameter, has been described in elderly subjects. Increased frequency of VRS dilatation with age was demonstrated in healthy subjects by Inglese et al. [12], whereas Rouhl et al. [13] suggest that the presence of dilated VRS correlates significantly not only with age, but also with hypertension, small lacunar infarcts and focal lesions of the white matter.

Two mechanisms potentially responsible for age-related dilatation of VRS are considered. The first concept is based on presumption that the ventricular system and subarachnoid space dilate with age, with consequent dilatation of

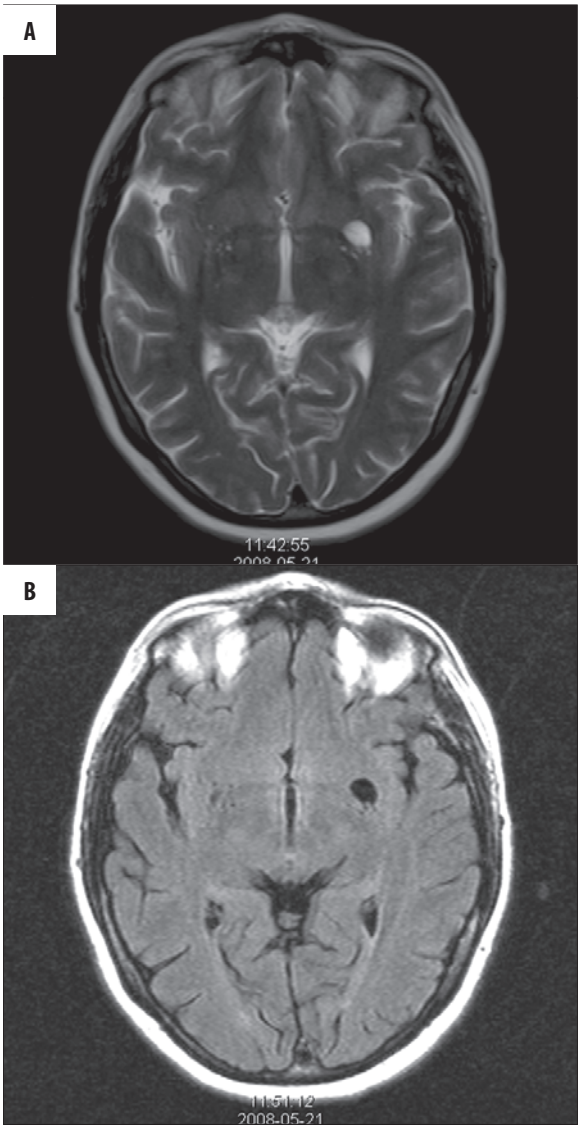

Figure 2. Multiple normal and single dilated VRS in the insular region in T2-weigthed image (**A**) and in FLAIR sequence (**B**).

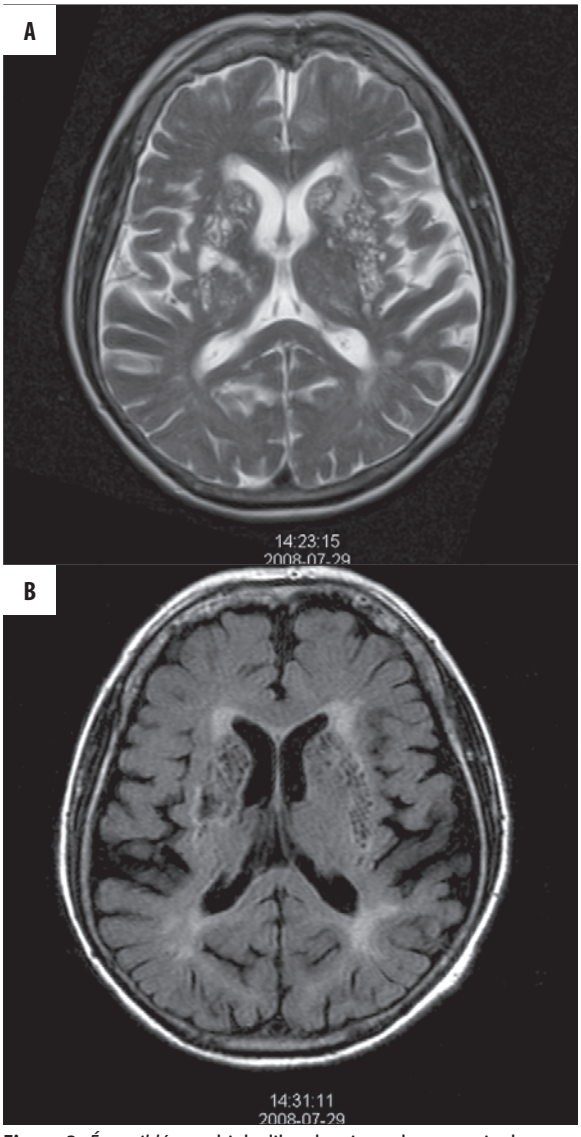

Figure 3. *État criblé* – multiple dilated perivascular spaces in the basal ganglia in T2-weighted image (**A**). In FLAIR image (**B**) hyperintense periventricular vascular infarction lesions are also seen.

perivascular spaces as the anatomic continuation of these structures. The second mechanism takes into account atherosclerotic changes common in elderly patients, even those without hypertension. Blood vessels become wider and more tortuous, which can explain increased amount of perivascular interstitium containing vacuoles and eventual dilatation of perivascular spaces [14].

„Dilatation", „accentuation", or „enlargement" of perivascular spaces are the terms often used in the descriptions of MRI results. The correctness of this terminology is disputable, as no uniform criteria concerning the size of normal and dilated VRS have been developed to date. According to Groeschel et al. [2], the presence of VRS in MR images is a normal phenomenon. The authors demonstrated that visualization of perivascular spaces is dependent on imaging technique and is increased in high-resolution MR sequences. Therefore, they claim that the main criterion of VRS dilatation should be the shape rather than size of these spaces. According to this opinion, the structures with segmental dilatation, irregular, „expanded", can be classified as dilated, whereas those with smooth and regular outlines should be classified as normal (Figure 2A,B). Additionally, to distinguish between enlarged VRS as an anatomic variants and as pathological signs, the condition of surrounding cerebral tissue and clinical presentation should be taken into consideration [2].

Multiple, dilated VRS present in the basal nuclei are referred to as „etat criblé" (Figure 3). In such cases, the arteries are dilated with wall sclerotization, and the perivascular tissue demonstrates gliosis zones extending along degenerated axons (Figure 4) [8].

Cyst-like VRS dilatations develop as a result of obstructed interstitial fluid outflow. In exterme cases, giant dilatation of Virchow-Robin spaces within the basal nuclei or the midbrain may cause compression of the aqueduct or ventricle III and symptomatic hydrocephalus, requiring treatment [8].

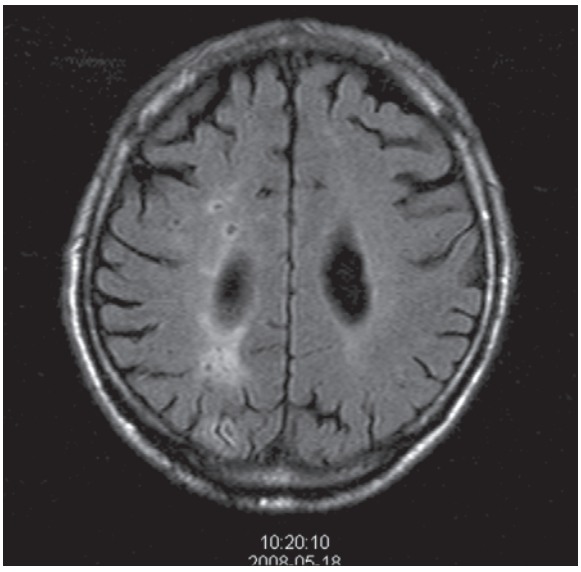

Figure 4. Dilated perivascular spaces could be surrounded by a gliosis zone well recognized in FLAIR images.

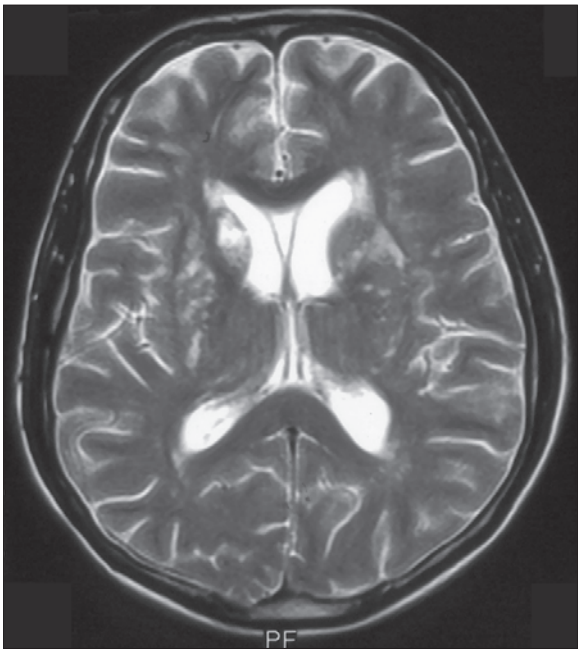

Figure 5. Enlarged perivascular spaces in the basal ganglia in a HIV-infected patient with cryptococcosis.

The literature includes several publications concerning giant cystic widening of Virchow-Robin spaces. Salzman et al. [15] described 37 cases of such abnormality. The changes were most frequently observed in the thalamo-mesencephalic region. In 9 cases, mass effect and hydrocephalus requiring surgical intervention was observed. Rohlfs et al. [13] reported two cases of VRS dilatation with giant tumor-mimicking cyst-like lesions located in the basal nuclei, accompanied by hydrocephalus.

Dilatation of perivascular spaces is in most cases diagnosed accidentally in imaging studies performed for other reasons. Initially it was associated with hypertension, dementia, epilepsy or migraine. However, no significant correlations between VRS dilatation and clinical symptoms have been demonstrated [7]. Non-specific symptoms include headaches; in a study by Salzman et al. [15] this symptom was observed in 50% of the examined patients.

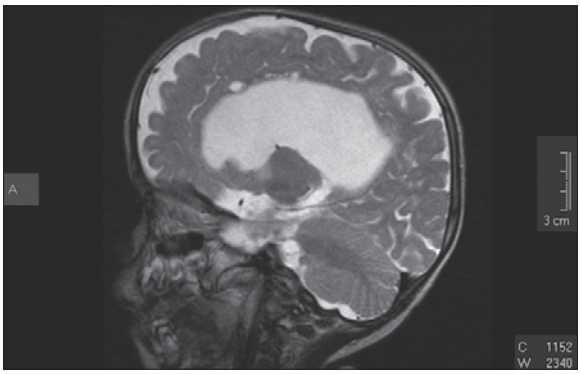

Figure 6. Prominent Virchow-Robin spaces in the corpus callosum in a child with Hurler type mucopolysaccharidosis.

Table 1. Syndromes and disorders associated with dilatation of perivascular spaces, modified according to Groeschel et al. [2].

Etiology	Syndromes and disorders
Metabolic/congenital	Mucopolysaccharidoses (Lowe) Oculocerebrorenal syndrome (Steinert) Myotonic dystrophy Coffin-Lowry syndrome
Vascular	CADASIL Migraine Vascular dementia
Inflammatory	Cryptococcosis Neurocysitcercosis Multiple sclerosis
Neuroectodermal	Eotodermal dysplasias Frontonasal dysplasia Jouber't syndrome
Neoplastic	Acute lymphoblastic leukemia
Miscellaneous	Parkinson disease Chronic alcoholism Traumatic brain injury

It has not been elucidated definitely whether VRS dilatation has any effect on brain function. Mathias et al. [16] failed to observe remodeling of cerebral cortex areas in fMRI performed in two patients with marked cyst-like dilatation of perivascular spaces. Also neuropsychiatric examinations revealed no abnormalities, only in tractography the diffusion tensor was found to be decreased in the investigated area. Similarly, Akter et al. [17] did not observe Wallerian degeneration of adjacent neural tracts in patients with VRS dilatation in diffusion tensor imaging. In contrast, Maclullich et al. [18], in a study of a large group of healthy subjects aged 65–70 demonstrated a correlation between VRS dilatation and deterioration of cognitive functions.

Table 2. Clinical symptoms observed in the course of mucopolysacchridoses, modified according to Barkovich [22].

Syndrome	Gene mapping	Extra-CNS symptoms	Neurological symptoms
MPS IH Hurler	4p16.3	Dwarfism, facial deformation, hepatosplenomegaly, bone defects, cardiac abnormalities, corneal opacification	Severe mental impairment, deafness, hydrocephalus
MPS IS Scheie	4p16.3	Abnormalities similar to IH, but less significant	Absent
MPS IH/S Hurler/Scheie	4p16.3	Phenotype intermediate between Hurler and Scheie types	Mild mental impairment, deafness, arachnoid cysts
MPS II Hunter A (severe)	Xq28	Phenotype similar to Hurler type without corneal opacification	Mental impairment, deafness, hydrocephalus
MPS II Hunter B (mild)	Xq28	Course slower than in II A, no corneal opacification	Normal mental development
MPS III Sanfilippo A, B, C, D	17q11-21	Facial features thickening, mild bone and interstitial organ abnormalities	Pronounced CNS symptoms - severe psychodegradation, behavioral changes, muscular weakness, seizures, pyramidal signs
MPS IV Morquio A	16q24.3	Bone deformation, odontoid hypoplasia, atlanto-axial subluxation, dwarfism, mitral insufficiency	Normal intelligence level, cervical spinal cord and nerve root compression, hearing impairment
MPS IV Morquio B	16q24.3	Symptoms like in type IV A, late corneal opacification	Mental retardation, deafness
MPS VI Maroteaux-Lamy	5q13-q14	Dysostosis multiplex, corneal opacification, hepatosplenomegaly	Normal intelligence level, spinal cord compression, hydrocephalus
MPS VII Sly	7q21-q22	Phenotype similar to MPS IH, later corneal opacification	Mental retardation, hydrocephalus

Dilatation of VRS can be associated with a number of pathologic processes. Cumurciuc et al. [19] observed increased occurrence of dilated VRS in patients with cerebral autosomal dominant cerebral arteriopathy with subcortical infarcts and leucoencephalopathy (CADASIL). The authors found no correlations between VRS dilatation and ischemic or hemorrhagic lesions, but emphasized their correlation with age and/or vascular wall damage associated with the pathology. Also Rouhlfs et al. [13] believed that the presence of dilated VRS could be a sign of small cerebral vessel pathology and a good predictor of development of clinically asymptomatic ischemic foci, whereas Inglese et al. [12] suggested that VRS dilatation might also be an early consequence of traumatic changes.

Dilatation of VRS can also be observed in inflammatory diseases – dilated, filled with fungal tissue and mucoid discharge perivascular spaces are one of the typical symptoms of cryptococcosis (Figure 5) [20]. Dilated VRS have also been observed in patients with adrenoleucodystrophy. According to Groeschel et al. [21], dilatation of perivascular spaces in such patients may reflect the perivascular inflammatory component. in mucopolysaccharidoses, the dilated VRS are filled with excess amounts of glycosaminoglycans (Figure 6) [3].

The diagnostics of dilatation of perivascular spaces is not difficult. However, other lesions mimicking VRS should be taken into consideration. Kwee et al. [3] mention the following conditions which should be considered in differential diagnosis: periventricular leukomalacia, SM, neurocysticercosis, aneurysmal tumors, arachnoid and neuroepithelial cysts [3]. The complete list of conditions that should be taken into account in differential diagnosis is presented in Table 1, whereas Table 2 includes short characteristics of symptoms observed in the course of mucopolysaccharidoses.

References:

1. Atlas SW, Lavi E: Intral-Axial Brain Tumors. Magnetic Resonance Imaging of the Brain and Spine. Second Edition. Lippincott-Raven Publishers, Philadelphia, 1996; 18: 806–7
2. Groeschel S, Chong WK, Surtees R et al: Virchow-Robin spaces on magnetic resonance images: normative data, their dilatation, and a review of the literature. Neuroradiology, 2006; 48: 745–54
3. Kwee RM, Kwee TC: Virchow-Robin spaces at MR imaging. Radiographics, 2007; 27: 1071–86
4. Krahn V: The pia at the site of the entry of blood vessels into the central nervous system. Anat Embryol, 1982; 164: 257–63
5. Ozturk MH, Aydingoz U: Comparsion of MR signal intensities of cerebral perivascular (Virchow-Robin) and subarachnoid spaces. J Comput Assist Tomogr, 2002; 26: 902–4
6. Pollock H, Hutchings M, Weller RO et al: Perivascular spaces in the basal ganglia of the human brain: the relationship to lacunes. J Anat, 1997; 191: 337–46

7. Mitsuyama Y: Cerebrovascular dementia; correlation of computed and histopathologic findings. Rinsho Hoshasem, 1989; 34: 1307–15
8. Marnet D, Noudel R, Peruzzi P et al: Dilatation of Virchow-Robin perivascular spaces (types III cerebral lacunae): radio-clinical correlation. Rev Neurol, 2007; 163: 561–71
9. Gross PM, Wall KM, Pang JJ et al: Microvascular specializations promoting rapid interstitial solute dispersion in nucleus tractus solitaruis. Am J Physiol, 1990; 259: 1131–18
10. Elster AD, Richardson DN: Focal high on MR scans of midbrain caused by enlarged perivascular spaces: MR-pathologic correlation. AJR Am J Roentgenol, 1991; 156: 157–60
11. Osborn AG et al: Diagnostic Imaging. Brain. Amirsys Inc., Salt Lake City, 2004
12. Inglese M, Bomsztyk E, Gonen O et al: Dilated perivascular spaces: hallmarks of mild traumatic brain injury. AJNR Am J Neuroradiol, 2005; 26: 719–24
13. Rohlfs J, Riegel T, Khalil M et al: Enlarged perivascular spaces mimicking multicystic brain tumors. Report of two cases and review of the literature. J Neurosurg, 2005; 102: 1142–46
14. Atlas SW, Lavi E: Intra-Axial Brain Tumors. Magnetic Resonance Imaging of the Brain and Spine. Second Edition. Lippincott-Raven Publishers, Philadelphia, 1996
15. Salzman KM, Osborn AG, House P et al: Giant tumefactive perivascular spaces. AJNR Am J Neuroradiol, 2005; 26: 298–305
16. Mathias J, Koessler L, Brissart H et al: Giant cystic widening of Virchow-Robin spaces: an anatomofunctional study. AJNR Am J Neuroradiol, 2007; 28: 1523–25
17. Akter M, Hirai T, Kitajima M et al: Multiple prominent dilated perivascular spaces do not induce Wallerian degeneration as evaluated by diffusion tensor imaging. AJNR Am J Neuroradiol, 2007; 28: 283–84
18. Macllulich AM, Wardlaw JM, Ferguson KJ et al: Enlarged perivascular spaces are associated with cognitive function in healthy elderly men. J Neurol Neurosurg Psychiatry, 2004; 75: 1516–17
19. Cumurciuc R, Guichard JP, Reizine D et al: Dilation of Virchow-Robin spaces in CADASIL. Eur J Neurol, 2006; 13: 187–90
20. Kovoor JM, Mahadevan A, Narayan JP et al: Cryptococcal choroid plexitis as a mass lesion: MR imaging and histopathologic correlation. AJNR Am J Neuroradiol, 2002; 23: 273–76
21. Groeschel S, Brockmann K, Hanefeld F et al: Virchow-Robin spaces on magnetic resonance images of children with adrenoleukodystrophy. Eur J Paediatr Neurol, 2007; 11: 142–45
22. Barkovich AJ: Pediatric neuroimaging. 2nd Edition. Raven Press, New York, 1995